chemistry, 2002, 41(14), 4503-4510); Genesis, volume 30, issue 3, 2001; Heasman, J., Dev. Biol., 2002, 243, 209-214; Nasevicius et al., Nat. Genet., 2000, 26, 216-220; Lacerra et al., Proc. Natl. Acad. Sci., 2000, 97, 9591-9596; and U.S. Pat. No. 5,034,506, issued Jul. 23, 1991. In some embodiments, the morpholino-based oligomeric compound is a phosphorodiamidate morpholino oligomer (PMO) (e.g., as described in Iverson, Curr. Opin. Mol. Ther., 3:235-238, 2001; and Wang et al., J. Gene Med., 12:354-364, 2010; the disclosures of which are incorporated herein by reference in their entireties).

[0104] Cyclohexenyl nucleic acid oligonucleotide mimetics are described in Wang et al., J. Am. Chem. Soc., 2000, 122, 8595-8602.

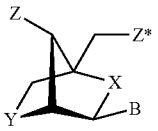
[0105] Modified oligonucleotide backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These comprise those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH2 component parts; see U.S. Pat. Nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437; and 5,677,439, each of which is herein incorporated by reference.

[0106] Modified oligonucleotides are also known that include oligonucleotides that are based on or constructed from arabinonucleotide or modified arabinonucleotide residues. Arabinonucleosides are stereoisomers of ribonucleosides, differing only in the configuration at the 2'-position of the sugar ring. In some embodiments, a 2'-arabino modification is 2'-F arabino. In some embodiments, the modified oligonucleotide is 2'-fluoro-D-arabinonucleic acid (FANA) (as described in, for example, Lon et al., Biochem., 41:3457-3467, 2002 and Min et al., Bioorg. Med. Chem. Lett., 12:2651-2654, 2002; the disclosures of which are incorporated herein by reference in their entireties). Similar modifications can also be made at other positions on the sugar, particularly the 3' position of the sugar on a 3' terminal nucleoside or in 2'-5' linked oligonucleotides and the 5' position of 5' terminal nucleotide.

[0107] PCT Publication No. WO 99/67378 discloses arabinonucleic acids (ANA) oligomers and their analogues for improved sequence specific inhibition of gene expression via association to complementary messenger RNA.

[0108] Other preferred modifications include ethylene-bridged nucleic acids (ENAs) (e.g., International Patent Publication No. WO 2005/042777, Morita et al., Nucleic Acid Res., Suppl 1:241-242, 2001; Surono et al., Hum. Gene Ther., 15:749-757, 2004; Koizumi, Curr. Opin. Mol. Ther., 8:144-149, 2006 and Horie et al., Nucleic Acids Symp. Ser (Oxf), 49:171-172, 2005; the disclosures of which are incorporated herein by reference in their entireties). Preferred ENAs include, but are not limited to, 2'-O,4'-C-ethylene-bridged nucleic acids.

[0109] Examples of LNAs are described in WO/2008/043753 and include compounds of the following general formula.



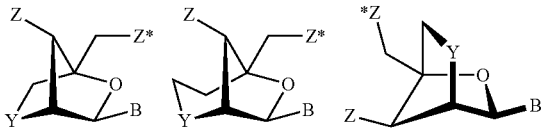
[0110] where X and Y are independently selected among the groups —O—,

[0111] —S—, —N(H)—, N(R)—, —CH_2— or —CH— (if part of a double bond),

[0112] —CH_2—O—, —CH_2—S—, —CH_2—N(H)—, —CH_2—N(R)—, —CH_2—CH_2— or —CH_2—CH— (if part of a double bond),

[0113] —CH═CH—, where R is selected from hydrogen and C_{1-4}-alkyl; Z and Z* are independently selected among an internucleoside linkage, a terminal group or a protecting group; B constitutes a natural or non-natural nucleotide base moiety; and the asymmetric groups may be found in either orientation.

[0114] Preferably, the LNA used in the oligonucleotides described herein comprises at least one LNA unit according any of the formulas



wherein Y is —O—, —S—, —NH—, or N(R^H); Z and Z* are independently selected among an internucleoside linkage, a terminal group or a protecting group; B constitutes a natural or non-natural nucleotide base moiety, and RH is selected from hydrogen and C_{1-4}-alkyl.

[0115] In some embodiments, the Locked Nucleic Acid (LNA) used in the oligonucleotides described herein comprises at least one Locked Nucleic Acid (LNA) unit according any of the formulas shown in Scheme 2 of PCT/DK2006/000512.

[0116] In some embodiments, the LNA used in the oligomer of the invention comprises internucleoside linkages selected from —O—$P(O)_2$—O—, —O—P(O,S)—O—, —O—$P(S)_2$—O—, —S—$P(O)_2$—O—, —S—P(O,S)—O—, —S—$P(S)_2$—O—, —O—$P(O)_2$—S—, —O—P(O,S)—S—, —S—$P(O)_2$—S—, —O—$PO(R^H)$—O—, O—PO(OCH_3)—O—, —O—$PO(NR^H)$—O—, —O—PO(OCH_2CH_2S—R)—O—, —O—$PO(BH_3)$—O—, —O—PO(NHR^H)—O—, —O—$P(O)_2$—NR^H—, —NR^H—$P(O)_2$—O—, —NR^H—CO—O—, where R^H is selected from hydrogen and C_{1-4}-alkyl.